

RESEARCH ARTICLE

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Cost Barriers and Health Literacy on Cholangiocarcinoma Rescreening Intention in Khon Kaen, Thailand: A Causal Mediation Analysis

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Abstract

Background: Cholangiocarcinoma (CCA) is a major public health issue in Southeast Asia and has the highest global incidence in Northeast Thailand. Thailand has implemented cholangiocarcinoma screening; nonetheless, public access to screening remains limited. This study aims to examine the impact of cost barriers on cholangiocarcinoma rescreening intention with a mediating effect of health literacy. **Methods:** This cross-sectional study was conducted with participants who received cholangiocarcinoma screening in four community hospitals between November and December 2024. The association between costs, health literacy, and rescreening intention was investigated through causal mediation analysis. **Results:** This study examined 171 participants; most participants were female (57.9%). Participants' rescreening intention was 71.9% (95%CI: 65.2% to 78.7%). Males intend to rescreen 75% more than females (69.7%). When quantifying the effect of costs channeled through health literacy to rescreening intention, 1) direct non-medical costs in the natural indirect effect showed statistically significant results at the lower to moderate cost levels. The results showed a statistically significant negative indirect effect at 300 THB (probability difference = -0.118, 95% CI: -0.182 to -0.055) and 500 THB (probability difference -0.135, 95% CI: -0.244 to -0.027). 2) Indirect costs in the natural indirect effect showed statistically significant results at the lowest levels. A statistically significant negative indirect effect was observed at 300 THB (probability difference -0.059, 95% CI: -0.095 to -0.023). **Conclusion:** Using health literacy as a mediator, direct non-medical costs and indirect cost expenses affect cholangiocarcinoma screening decisions. Expanding screening to communities, minimizing costs, and increasing health literacy on cholangiocarcinoma may increase screening.

Keywords: Cost, Health Literacy, Rescreening, Opisthorchis, Cholangiocarcinoma

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Introduction

Cholangiocarcinoma (CCA) is a major public health issue in Southeast Asia, having the highest global incidence in Northeast Thailand. The age-standardized rates (ASRs) for both sexes in Thailand were 8.9 per 100,000 person-years in 2021. The Northeastern has the highest ASR at 13.4 per 100,000 person-years [1]. This geographic concentration is connected to chronic *Opisthorchis viverrini* (OV) liver fluke infection. Raw or undercooked fish is still eaten in Khon Kaen province, an important endemic area. Due to advanced diagnosis, the mortality rate remains high despite decades of control efforts. Early diagnosis with ultrasound screening is the best way to increase high-risk population survival [2-4].

Thailand established the Cholangiocarcinoma Screening and Care Program (CASCAP), a prospective cohort research, to address the elevated prevalence of cholangiocarcinoma in northeastern Thailand. The project comprises community-level screening of populations at risk, the implementation of an online database, and ongoing monitoring [5]. The research indicated that the screening cohort showed a higher probability of identifying cholangiocarcinoma compared to the walk-in cohort, suggesting that ultrasound screening is an effective instrument for early diagnosis [4, 6]. Due to the slow progression of cholangiocarcinoma, prolonged monitoring is essential for early identification. Early detection of cholangiocarcinoma markedly improves patient survival rates [7].

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Financial limitations are often identified as an important barrier to medical adherence, though in nations such as Thailand that possess a Universal Health Coverage (UHC) system [8, 9]. The government covers direct medical costs, ‘cost barriers’ in this context pertain to direct non-medical expenses [7, 10]. Although ultrasound scans are offered at no charge, rural households continue to incur significant direct non-medical costs and indirect costs. This encompasses the costs related to long-distance travel to hospitals, food, accommodation, and the considerable opportunity cost of losing daily agricultural or employment income [8, 11]. These hidden costs can outweigh the perceived benefits of a preventive screening for cholangiocarcinoma when no symptoms are present leading to a non-screening intention to rescreen.

Health literacy (HL) is crucial in how individuals overcome these barriers and recognize the importance of preventive care. Health literacy (HL) comprises the cognitive and social competencies that allow individuals to get, understand and utilize health information to preserve their well-being [12, 13]. Prior research indicates that persons with sufficient health literacy (AHL) are correlated with greater participation in cancer screening [14–16]. The people with greater AHL may distinguish between essential and non-essential expenses and evaluate costs relative to health benefits and long-term risk reduction.

Previous research in Thailand has been focused on a single study on the cost-effectiveness analysis of ultrasound surveillance for cholangiocarcinoma [17]. Although the functions of cost and health literacy have been recognized, there remains a paucity of research investigating the causal mechanisms by which these factors interact to affect screening behavior. It is plausible that health literacy not only interacts with cost barriers but also functions as a mediator that transmits or decreases their effects. To clarify this complex mechanism, this study applied a causal mediation analysis. Unlike traditional association studies, causal mediation analysis provides a robust statistical framework to disentangle the pathways by estimating both the direct effect of cost barriers on intention and the indirect effect mediated by health literacy. Therefore, this study aims to apply this technique to examine the impact of cost barriers on cholangiocarcinoma rescreening intention in Khon Kaen, with a particular focus on analyzing the mediating effect of health literacy.

Materials and Methods

Study Design and Participants

This cross-sectional design study population in the target area comprised 570 individuals who had undergone screening for liver fluke and cholangiocarcinoma in Khon Kaen Province. To determine a representative sample size, the formula by Hsieh et al. [18] was employed, resulting in a calculated requirement of 179 participants.

These individuals were selected through a multistage random sampling process, which first involved a stratified selection of community hospitals from the northern, southern, central, and western zones, followed by simple random sampling within each hospital proportional to

its population. Ultimately, a total of 171 participants, or 95.53% of the target sample, voluntarily consented to take part in the research. Inclusion criteria were restricted to literate adults aged 18 years or older who had participated in at least one cholangiocarcinoma screening that focused on any of the following: verbal interview, urine testing, stool examination, or abdominal ultrasound, while the study excluded any individuals who were unwilling to cooperate with the data collection process.

Instrument

Data collection was conducted using structured questionnaires focusing on three primary areas. The main interest factor: Cost per screening visit was recorded in Thai Baht (THB) which 10.245 THB = 1 PPP-USD in 2025 based on IMF 2025 [19]. Indirect costs were categorized into two components: (1) productivity loss of service recipients and (2) productivity loss of caregivers. Direct non-medical costs including (1) travel expenses, and (2) additional food costs. The study outcome: The cholangiocarcinoma rescreening intention. Mediator, the research instrument was self-developed and adapted from the concepts of Nutbeam D. [20] and Tanasugarn C. [21]. Health literacy was evaluated across multiple dimensions, including information access, cognitive understanding, communication, and decision-making skills, as well as self-management and media literacy. Health literacy using questions on a 4-point Likert scale (1: very difficult, 2: difficult, 3: easy, 4: very easy). The health literacy levels were determined based on the average health literacy scores, categorized according to Tanasugarn C. [21] as follows: 1) Inadequate health literacy (a total score < 75%), and 2) Adequate health literacy (a total score ≥ 75%). Confounding factors: The potential factors were included as confounding factors in the analysis: adjusted by age, education, and income.

Quality Assessment of the Research Instruments; 1) Content Validity: The structured questionnaire was validated for content validity by three experts (one health economist, one specialist in medicine, and one statistician). All 45 items met the Item-Objective Congruence (IOC) index criteria. Specifically, 33 items (73.33%) had an IOC score of 1.00, while 12 items (26.67%) had a score of 0.67. The questionnaire and interview guidelines were subsequently revised and refined according to the experts’ recommendations. 2) Reliability: The questionnaire was tried out with 30 participants who shared similar characteristics with the target sample but resided in a different area. The results indicated that the Cronbach’s alpha coefficient for the health literacy section demonstrated 0.96.

The researchers requested cooperation from public health officials in charge of the liver fluke and cholangiocarcinoma screening to distribute the questionnaires to the target sample. If the participants were willing to respond, they could complete each section of the questionnaire at their own convenience. Data were collected between November and December 2024.

Data Analysis

Participant characteristics, cholangiocarcinoma

rescreening intention, costs, and health literacy levels were analyzed using descriptive statistics. Continuous variables were presented as means and standard deviations (SD), and medians and interquartile ranges (IQR) were additionally reported for skewed data. Categorical variables were expressed as frequencies and percentages. For the comparative analysis of participant characteristics between groups, the Chi-square test or Fisher's exact test was used for categorical variables, and the independent t-test or Mann-Whitney U test was applied for continuous variables depending on the data distribution.

Causal Mediation Analysis (CMA), based on the potential outcomes' framework [22], was utilized to investigate whether health literacy mediates the relationship between costs and cholangiocarcinoma rescreening intention. This method decomposes the total effect (TE) into: (1) the natural indirect effect (NIE), which captures the impact transmitted through health literacy, and (2) the natural direct effect (NDE), representing the direct influence of costs independent of the mediator ($TE = NIE + NDE$).

Analyses used predefined cost cut-points to explore variations in causal effects across the spectrum of financial burden. The effect of cost was estimated relative to a 0 THB baseline. Natural indirect, natural direct, and total effects were reported as probability differences with 95% CIs. Data processing and estimation were performed using StataNow 19.5 (StataCorp LLC, College Station, TX).

Ethical Considerations

This study was approved from the Human Research Ethics Committee of Khon Kaen University on October 21, 2024, approval number HE672192. These principles include respect for human dignity, informed consent through enough knowledge and autonomy in decision-making, and privacy and confidentiality before conducting research.

Results

Patient Characteristics

This study examined 171 participants, the non-intention to rescreen group was older, with 62.5% over 60 compared to 44.72%. Most participants were female (57.9%), with 62.5% declining non-intention to rescreen vs. 56.1%. The non-intention to rescreen group had more married people (91.7% vs. 75.6%).

Both groups had similar education, occupation, and income. Most participants (65.5%) had lower secondary education, worked in agriculture (80% in both groups), and earned 5,000 THB or less per month (83.0%). Mean monthly income was similar for non-intention to rescreen and intention to rescreen (4,070.83 and 4,191.06 THB, respectively) (Table 1).

Participants rescreening intention was 71.9% (95%CI: 65.2% to 78.7%). Male intention to rescreen 75% more than female (69.7%) (Table 2). The overall health literacy was adequate level (mean = 3.39 ± 0.41 out of maximum score). Decision Skills mean scored highest (3.46 ± 0.45) and Communication Skills rated lowest (3.27 ± 0.58) with the most variation. Other domains ranged from 3.37 to

3.45 (Table 3).

Causal mediation analysis: direct non-medical costs

The causal mediation analysis was performed to explore the role of health literacy in the relationship between direct non-medical costs and intending to receive service. The analysis used the probability difference to estimate the controlled effects, adjusted for age, education, and income. The results are summarized in Table 4, with 0 THB serving as the reference cost level.

Total effect

The analysis of the total effect indicated that direct non-medical costs had a statistically significant impact on the intention to receive service only at the highest level of cost. Specifically, the cost of 1,500 THB resulted in a statistically significant positive total effect (probability difference = 0.184, 95%CI: 0.076 to 0.293).

Natural direct effect

The natural direct effect, representing the portion of the relationship between costs and service intention that flows through pathways not involving health literacy, was not statistically significant at any level of direct non-medical costs (ranging from 300 THB to 1,500 THB).

Natural indirect effect

In contrast, the natural indirect effect, which quantifies the effect of costs channeled through health literacy, showed statistically significant results at the lower to moderate cost levels. The results showed a statistically significant negative indirect effect at 300 THB (probability difference = -0.118, 95%CI: -0.182 to -0.055) and 500 THB (probability difference = -0.135, 95%CI: -0.244 to -0.027) (Table 4).

Causal mediation analysis: indirect costs

The causal mediation analysis was performed to explore the role of health literacy in the relationship between indirect costs and intending to receive service. The analysis used the probability difference to estimate the controlled effects, adjusted for age, education, and income. The results are summarized in Table 5, with 0 THB serving as the reference cost level.

Total effect

The analysis of the total effect indicated that indirect costs had a statistically significant impact on the intention to receive service only at the highest level of cost. Specifically, the cost of 1,000 THB resulted in a statistically significant positive total effect (probability difference = 0.268, 95% CI: 0.146 to 0.391).

Natural direct effect

The natural direct effect, representing the portion of the relationship between costs and service intention that flows through pathways not involving health literacy, was found to be a positive direct effect at 300 THB (probability difference = 0.091, 95% CI: 0.014 to 0.167) and at 500 THB (probability difference = 0.146, 95% CI: 0.018 to 0.273).

Table 1. Characteristics of Participants Categorized by Intention to Rescreen (n = 171)

Characteristics	Total (n = 171)		Intention to rescreen (n = 123)		Non-intention to rescreen (n = 48)		p-value
	n	%	n	%	n	%	
Gender							0.446 ^a
Male	72	42.1	54	43.9	18	37.5	
Female	99	57.9	69	56.1	30	62.5	
Age (years)							0.072 ^a
< 50	48	28.1	36	29.3	12	25	
50 – 59	38	22.2	32	26	6	12.5	
> 60	85	49.7	55	44.7	30	62.5	
Mean (SD)	59.56	10.5	58.67	10.36	61.83	10.63	0.082 ^b
Education level							0.202 ^a
Lower secondary education or less	112	65.5	77	62.6	35	72.9	
Upper secondary education and beyond	59	34.5	46	37.4	13	27.1	
Occupational							0.359 ^c
Agriculture	136	79.5	98	79.7	38	79.2	
Government Official	10	5.9	5	4.1	5	10.4	
Merchant	3	1.8	3	2.4	0	0	
Private Sector Employee	4	2.3	4	3.2	0	0	
Other	18	10.5	13	10.6	5	10.4	
Marital status							0.051 ^a
Single	19	11.1	16	13	3	6.2	
Married	137	80.1	93	75.6	44	91.7	
Divorced/Separated/ Widowed	15	8.7	14	11.4	1	2.1	
Income (THB per month)							0.697 ^a
0 – 5,000	142	83	103	83.7	39	81.3	
> 5,001	29	17	20	16.3	9	18.7	
Mean (SD)	4157.31	3026.08	4191.06	3347.28	4070.83	2006.9	0.774 ^b
Median (IQR)	3600	2400	3600	2400	3800	2000	0.540 ^d

^a, Chi-square test; ^b, independent t-test; ^c, Fisher's exact test; ^d, Mann-Whitney U test

Table 2. The Cholangiocarcinoma Intention to Rescreen Screening (n = 171)

Screening	Male		Female		Overall		95%CI
	n	(%)	n	(%)	n	(%)	
Intention to rescreen	54	75	69	69.7	123	71.9	65.2 to 78.7
Non-intention to rescreen	18	25	30	30.3	48	28.1	21.3 to 34.8

Natural indirect effect

In contrast, the natural indirect effect, which quantifies the effect of costs channeled through health literacy, showed statistically significant results at the lowest levels. A statistically significant negative indirect effect was observed at 300 THB (probability difference = -0.059, 95% CI: -0.095 to -0.023) (Table 5).

Discussion

Most of the participants decided to re-attend the screening. 75% of males choose to re-attend compared to 69.7% of females. This may be attributed to the fact that cholangiocarcinoma are serious diseases that are challenging to manage once recognized, however, they

Table 3. Health Literacy Score (n = 171)

Health Literacy	Mean (SD)	95%CI	Health literacy levels
Access	3.45 (0.42)	3.39 to 3.51	Adequate
Cognitive	3.42 (0.39)	3.36 to 3.48	Adequate
Communication Skill	3.27 (0.58)	3.18 to 3.36	Adequate
Decision Skill	3.46 (0.45)	3.39 to 3.53	Adequate
Self-management and Media Literacy	3.37 (0.46)	3.30 to 3.44	Adequate
Overall	3.39 (0.41)	3.33 to 3.45	Adequate

Table 4. Adjusted Causal Mediation Effects of Direct Non-Medical Costs on Intending to Receive Service (n=171)

Direct non-medical costs		Probability difference	95%CI	p-value
THB	PPP-USD			
Total effect				
	Reference = 0			
300	29.28	-0.105	-0.210 to 0.0001	0.050
500	48.8	-0.12	-0.292 to 0.052	0.172
1000	97.61	0.087	-0.172 to 0.347	0.509
1500	146.41	0.184	0.076 to 0.293	0.001
Natural direct effect				
	Reference = 0			
300	29.28	0.013	-0.071 to 0.098	0.755
500	48.8	0.015	-0.148 to 0.178	0.855
1000	97.61	-0.039	-0.534 to 0.457	0.879
1500	146.41	-0.155	-0.927 to 0.617	0.695
Natural indirect effect				
	Reference = 0			
300	29.28	-0.118	-0.182 to -0.055	<0.001
500	48.8	-0.135	-0.244 to -0.027	0.014
1000	97.61	0.126	-0.392 to 0.644	0.634
1500	146.41	0.339	-0.375 to 1.053	0.352

* Probability differences were adjusted by age, education, and income; * 10.245 THB = 1 PPP-USD in 2025 (IMF, 2025)

Table 5. Adjusted Causal Mediation Effects of Indirect Costs on Intending to Receive Service (n=171)

Indirect costs		Probability difference	95%CI	p-value
THB	PPP-USD			
Total effect				
	Reference = 0			
300	29.28	0.031	-0.054 to 0.117	0.472
500	48.8	0.099	-0.033 to 0.230	0.143
1000	97.61	0.268	0.146 to 0.391	<0.001
Natural direct effect				
	Reference = 0			
300	29.28	0.091	0.014 to 0.167	0.02
500	48.8	0.146	0.018 to 0.273	0.025
1000	97.61	0.206	-0.053 to 0.465	0.119
Natural indirect effect				
	Reference = 0			
300	29.28	-0.059	-0.095 to -0.023	0.001
500	48.8	-0.047	-0.117 to 0.023	0.187
1000	97.61	0.062	-0.137 to 0.261	0.541

* Probability differences were adjusted by age, education, and income; * 10.245 THB = 1 PPP-USD in 2025 (IMF, 2025)

present an opportunity for successful treatment when identified in the early stages. Consequently, individuals prioritize screening as overall resulting in 71.9% deciding to participate in subsequent screenings. This corresponds with research indicating a greater percentage of individuals participating in cancer screening visits relative to those who do not attend [6, 23]. This could result from varying perceptions and awareness regarding the disease's seriousness, leading to some research indicating that fewer

than half of participants underwent screening for other cancer types [16, 24-26]. Furthermore, research indicates a higher incidence and greater involvement in screening and treatment among males compared to females. These disparities may stem from physiological differences in hormones and body composition, as well as varying levels of seriousness and awareness [27, 28].

Direct non-medical costs causal mediation analysis: the natural direct effect represented was not statistically

significant to service intention at any level of direct non-medical costs (ranging from 300 THB to 1,500 THB). However, the natural indirect effect, which quantifies the effect of costs channeled through health literacy showed statistically significant results at the lower to moderate cost levels. The results showed a statistically significant negative indirect effect at 300 THB and 500 THB. The study findings indicate that a direct non-medical spending increase and a high health literacy score result in lowered screening visits. This indicates that, despite a high health literacy score, direct non-medical costs continue to be a substantial factor affecting the decision to pursue screening services. Highly literate individuals might be making a more calculated economic decision or perceiving the risk differently. The existence of direct non-medical costs influences the decision to pursue screening once more. This conclusion aligns with research indicating that direct non-medical expenses influence the propensity to pursue healthcare services [8, 9]. Moreover, research indicates that direct non-medical expenses, especially long-distance travel, lead to a reduction in visits compared to shorter travel distances [29].

Indirect costs causal mediation analysis: the natural direct effect, representing the portion of the relationship between costs and service intention that flows through pathways not involving health literacy, was found to be a positive direct effect at 300 THB and at 500 THB. In contrast, the natural indirect effect, which quantifies the effect of costs channeled through health literacy, showed statistically significant results at the lowest levels. A statistically significant negative indirect effect was observed at 300 THB. Research reveals that both indirect costs and health literacy diminish the likelihood of pursuing screening. When prioritizing low indirect costs, patients are still inclined to pursue further screening, this aligning with research indicating that cost affects cancer patients' decisions to seek medical care [8]. Previous research indicates that although indirect costs may directly hinder access to services, individuals prioritize the scheduling of appointments and receiving of treatment over the conservation of indirect charges [30, 31]. Nonetheless, as indirect costs rise and the HL score escalates, a decreased number of patients return for screening. Increased indirect expenses may lead those capable of self-assessing their health to hesitate, experience anxiety, or fear undertaking screening [32, 33], or to fear the possibility of detecting an illness [34]. This category comprises those receiving welfare benefits and those with the financial capacity to obtain screenings from other medical institutions, along with individuals who have previously undergone screening, which could contribute to a decreased attendance rate for follow-up screenings.

In conclusion, when considering health literacy as a mediator, both direct non-medical costs and indirect costs are associated with the decision to pursue future cholangiocarcinoma screening. Expanding screening efforts to communities and minimizing both direct, non-medical, and indirect costs for individuals undergoing screening, such as providing more mobile screening units or community-based along with providing health literacy

regarding cholangiocarcinoma, may facilitate sustained participation in screening programs.

Limitations of the study

The cross-sectional approach restricts our capacity to determine the causal relationship among factors and cholangiocarcinoma screening intention to rescreen. Its nature indicates a specific point in time that may differ from long-term economic trends. Although we adjusted for several significant confounders (age, education, and income), unmeasured characteristics such as social support and quality of life may have impacted screening intention to rescreen. Finally, the limited prior research on cost barriers and health literacy in the screening of cholangiocarcinoma limits the comparative study of this subject. Intention to re-screen serves only as a proxy for actual behavior and may be influenced by social desirability bias.

Author Contribution Statement

SP, and JR designed and conceptualized the study. PS and SP were involved in the data-cleaning process, data analysis process, and interpreting the results. PS, SP, NS, NHP, and PB led the manuscript writing process with support from JR. All the authors reviewed and contributed to the writing and have approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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